Citrate homeostasis and trafficking in osmoadadaptive response of

Saccharomyces cerevisiae

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Inter-organellar cross talk is an important component of cellular stress response allowing adaptation and survival under different unfavourable conditions. In our laboratory we are studying the peroxisomes-mitochondria communication during osmotic stress induced by sodium chloride in *Saccharomyces cerevisiae* cells. We demonstrated that osmotic stress activates the mitochondrial retrograde (RTG) pathway in WT cells, as indicated by *CIT2* upregulation, encoding the peroxisomal citrate synthase, a prognostic marker of RTG activation. Interestingly, metabolomic quantification of TCA cycle intermedia showed that in WT cells treated with NaCl, intracellular citrate levels are increased compared to control cells. The synthesis of citrate mainly derives from peroxisomes, as indicated by the up regulation of *CIT2*, and not of *CIT1* and *CIT3*. Furthermore, the involvement of the mitochondrial citrate transporter, encoded by *YHM2*, in the osmoadaptive response, is demonstrated and preliminary results suggested that there is a modulation of cytosolic NADP-specific isocitrate dehydrogenase Idp2p activity. We propose that under NaCl-induced stress, RTG-dependent citrate synthesis occurs mainly in peroxisomes and cytosol. Cytosolic citrate might be converted to 2-oxoglutarate by Idp2p and then imported into mitochondria via the Yhm2 carrier in exchange with citrate. This would allow the replenishment of TCA cycle with 2-oxoglutarate. In the absence of *YHM2*, alternative pathways might be activated with the involvement of the mitochondrial transporter Odc2 for transport of 2-oxoglutarate in exchange with malate. Our data reveals a new layer of metabolic coordination among organelles and identifies citrate shuttling as a crucial adaptive mechanism upon osmotic stress.